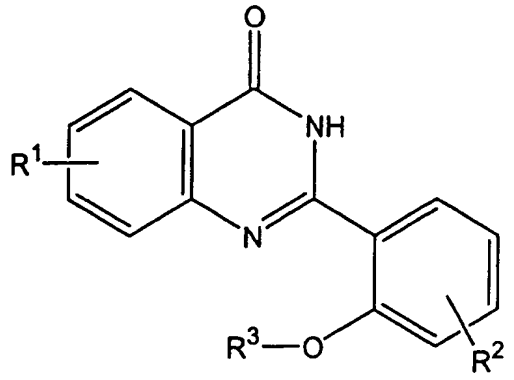
Amendments to the Claims

This listing of claims will replace all prior versions, and listing, of claims in the application.

Listing of Claims

1-49. (Canceled)

50 (Currently amended). A method of in-vivo localizing a substantially water-insoluble drug within the extracellular space ~~a~~ of solid tumor tissue in an animal, the method comprising administering a water-soluble prodrug to the animal, wherein the prodrug comprises the drug substituted with a prosthetic group that is cleavable by an enzyme, which ~~that~~ is present in the extracellular space of the tumor and ~~that~~ which is produced naturally by cells of the tumor, wherein the enzyme is unique to tumor cells or is produced at concentrations that are higher than that in normal tissues, whereby cleavage of the prosthetic group from the prodrug yields the substantially water-insoluble drug entrapped in the extracellular space, wherein the prodrug has the structure



wherein

R^1 is selected from the group consisting of a hydrogen radical, a radionuclide, a molecule labeled with one or more radionuclides, a boron atom, a molecule labeled with one or more boron atoms, and a boron cage;

R^2 is selected from the group consisting of a hydrogen radical, a radionuclide, and a boron cage;

at least one of R^1 and R^2 is not a hydrogen radical; and

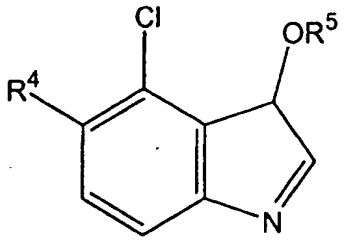
R^3 is a prosthetic group that can be cleaved from the prodrug by the enzyme.

51 (Previously presented). The method of claim 50, wherein R^1 is a hydrogen radical and R^2 is a radionuclide.

52 (Previously presented). The method of claim 50, wherein R^1 is a radionuclide and R^2 is a hydrogen radical.

53 (Previously presented). The method of claim 50, wherein R^3 is a phosphate moiety.

54 (Currently amended). A method of in-vivo localizing a substantially water-insoluble drug within the extracellular space ~~a~~ of solid tumor tissue in an animal, the method comprising administering a water-soluble prodrug to the animal, wherein the prodrug comprises the drug substituted with a prosthetic group that is cleavable by an enzyme, which ~~that~~ is present in the extracellular space of the tumor and ~~that~~ which is produced naturally by cells of the tumor, wherein the enzyme is unique to tumor cells or is produced at concentrations that are higher than that in normal tissues, whereby cleavage of the prosthetic group from the prodrug yields the substantially water-insoluble drug entrapped in the extracellular space, wherein the prodrug has the structure



wherein

R^4 is selected from the group consisting of a radionuclide, a molecule labeled with one or more radionuclides, a boron atom, a molecule labeled with one or more boron atoms, and a boron cage, and

R^5 is a prosthetic group that can be cleaved from the prodrug by the enzyme.

55. (Withdrawn) The method of claim 54, wherein R^4 is a radionuclide and R^5 is a beta-D-galactosyl moiety.

56. (Withdrawn) The method of claim 50, wherein R^3 is a sulfate moiety.

57. (Withdrawn) The method of claim 50, wherein R^3 is a peptide moiety.

58. (Withdrawn) The method of claim 50, wherein R^3 is a sugar moiety.

59 (Previously presented). The method of claim 50, wherein the enzyme is present in the extracellular space of the tumor at concentrations higher than in the extracellular space of normal tissues.

60 (Previously presented). The method of claim 50, wherein the enzyme is selected from the group consisting of an acetylglucosaminidase, an acetylneuraminidase, an aldolase, an amidotransferase, an arabinopyranosidase, a carboxykinase, a cellulase, a deaminase, a decarboxylase, a dehydratase, a dehydrogenase, a DNAse, an endonuclease, an epimerase, an esterase, an exonuclease, a fucosidase, a galactosidase, a glucokinase, a glucosidase, a glutaminase, a glutathionase, a glucoronidase, a guanidinobenzoatase, a hexokinase, an iduronidase, a kinase, a lactase, a mannosidase, a nitrophenylphosphatase, a peptidase, a peroxidase, a phosphatase, a phosphotransferase, a protease, an RNAse, a reductase, a sulfatase, a telomerase, a transaminase, a transcarbamylase, a transferase, a xylosidase, a uricase, and a urokinase.

61 (Previously presented). The method of claim 50, wherein the prodrug is either injected by a route selected from the group consisting of intravenously, infra-arterially, subcutaneously, into the lymphatic circulation, intraperitoneally, intrathecally, intratumorally, and intravesically, or is given orally.

62 (Previously presented). The method of claim 50, wherein the drug comprises a radionuclide.

63 (Previously presented). The method of claim 62, wherein the radionuclide is selected from the group consisting of a gamma emitting radionuclide, a positron emitting radionuclide, an alpha particle emitting radionuclide, and a beta particle emitting radionuclide.

64 (Withdrawn). The method of claim 63, wherein the radionuclide is an alpha particle emitting radionuclide selected from the group consisting of astatine-211, bismuth-212, and bismuth-213.

65 (Withdrawn). The method of claim 64, wherein the beta particle emitting radionuclide emits beta particles whose energies are greater than 1 keV.

66 (Withdrawn). The method of claim 63, wherein the beta particle emitting radionuclide is iodine-131, copper-67, samarium-153, gold-198, palladium-109, rhenium-186, rhenium-188, dysprosium-165, strontium-89, phosphorous-32, phosphorous-33, or yttrium-90.

67 (Withdrawn). The method of claim 50, wherein the drug comprises a boron cage.

68 (Previously presented). The method of claim 50, wherein the prosthetic group is a phosphate group.

69 (Withdrawn). The method of claim 50, wherein the prosthetic group is a sulfate group.

70 (Withdrawn). The method of claim 50, wherein the prosthetic group is a glycoside.

71 (Withdrawn). The method of claim 50, wherein the prosthetic group is a monosaccharide.

72 (Withdrawn). The method of claim 50, wherein the prosthetic group is a polysaccharide.

73 (Withdrawn). The method of claim 50, wherein the prosthetic group is an aromatic moiety.

74 (Withdrawn). The method of claim 50, wherein the prosthetic group is an amino acid moiety.

75 (Withdrawn). The method of claim 50, wherein the prosthetic group is a polypeptide.

76 (Previously presented). The method of claim 54, wherein the enzyme is present in the extracellular space of the tumor at concentrations higher than in the extracellular space of normal tissues.

77 (Previously presented). The method of claim 54, wherein the enzyme is selected from the group consisting of an acetylglucosaminidase, an acetylneuraminidase, an aldolase, an amidotransferase, an arabinopyranosidase, a carboxykinase, a cellulase, a deaminase, a decarboxylase, a dehydratase, a dehydrogenase, a DNAse, an endonuclease, an epimerase, an esterase, an exonuclease, a fucosidase, a galactosidase, a glucokinase, a glucosidase, a glutaminase, a glutathionase, a glucoronidase, a guanidinobenzoatase, a hexokinase, an iduronidase, a kinase, a lactase, a mannosidase, a nitrophenylphosphatase, a peptidase, a peroxidase, a phosphatase, a phosphotransferase, a protease, an RNAse, a reductase, a sulfatase, a telomerase, a transaminase, a transcarbamylase, a transferase, a xylosidase, a 'incase, and a urokinase.

78 (Previously presented). The method of claim 54, wherein the prodrug is either injected by a route selected from the group consisting of intravenously, intra-arterially, subcutaneously, into the lymphatic circulation, intraperitoneally, intrathecally, intratumorally, and intravesically, or is given orally.

79 (Previously presented). The method of claim 54, wherein the drug comprises a radionuclide.

80 (Previously presented). The method of claim 79, wherein the radionuclide is selected from the group consisting of a gamma emitting radionuclide, a positron emitting radionuclide, an alpha particle emitting radionuclide, and a beta particle emitting radionuclide.

81 (Withdrawn). The method of claim 80, wherein the radionuclide is an alpha particle emitting radionuclide selected from the group consisting of astatine-211, bismuth-212, and bismuth-213.

82 (Withdrawn). The method of claim 81, wherein the beta particle emitting radionuclide emits beta particles whose energies are greater than 1 keV.

83 (Withdrawn). The method of claim 80, wherein the beta particle emitting radionuclide is iodine-131, copper-67, samarium-153, gold-198, palladium-109, rhenium-186, rhenium-188, dysprosium-165, strontium-89, phosphorous-32, phosphorous-33, or yttrium-90.

84 (Withdrawn). The method of claim 54, wherein the drug comprises a boron cage.

85 (Previously presented). The method of claim 54, wherein the prosthetic group is a phosphate group.

86 (Withdrawn). The method of claim 54, wherein the prosthetic group is a sulfate group.

87 (Withdrawn). The method of claim 54, wherein the prosthetic group is a glycoside.

88 (Withdrawn). The method of claim 54, wherein the prosthetic group is a monosaccharide.

89 (Withdrawn). The method of claim 54, wherein the prosthetic group is a polysaccharide.

90 (Withdrawn). The method of claim 54, wherein the prosthetic group is an aromatic moiety.

91 (Withdrawn). The method of claim 54, wherein the prosthetic group is an amino acid moiety.

92 (Withdrawn). The method of claim 54, wherein the prosthetic group is a polypeptide.